REMARKS

Interview

Applicants would like to thank Examiner Wang and Supervisory Examiner Andres for the phone conference held with Applicants' representative. During the phone conference, proposed amendments to the claims for overcoming the rejections were discussed. Applicants have considered the proposed amendments and have incorporated some of the amendments into the claims. Also, arguments for overcoming the art rejections were discussed. Applicants have incorporated these arguments into the present response.

Status of the Claims

Claims 93-102, 139-142, 144-154, 156, and 174-189 are currently pending in the present application. Claims 1-92, 103-138, 143, 155, and 157-173 have been canceled without prejudice or disclaimer of the subject matter claimed therein. Claims 93, 98, 102, 139, 141, 142, 144, 145, 151-154, and 156 have been amended, and new claims 174-189, directed to the same invention as claims 93-102, 139-142, 144-154, 156, and 174-189 have been added.

Amendments to the Claims

The amendments to claims 93, 98, 102, 139, 141, 142, 144, 145, 151-154, and 156 do not introduce prohibited new matter. Representative support for the amendments to these claims can be found throughout the specification.

Claims 93, 98, 139, 141, 144, 145, 151-154, and 156 have been amended to delete the phrase "or fragment thereof."

Claim 93 has been amended to insert the phrase "by comparing with binding of LEV to the SV2 protein." Representative support for the insertion can be found on page 18, lines 5-24.

Support for the amendment to claims 102 and 142 can be found on page 13, lines 10-23.

Support for the amendment to claims 139 and 156 can be found in claim 155 as originally filed.

New claims 174-189 have been added to more clearly define the claimed invention. They do not introduce prohibited new matter.

Representative support for new claims 174, 175, 179, 180, 185, and 186 can be found on page 13, lines 10-23.

Representative support for new claims 176, 181, and 187 can be found on page 13, lines 10 and 11.

Representative support for new claims 177, 178, 182, 183, 188, and 189 can be found on page 27, lines 16-20.

Claim Objections

Claims 95 and 155 are objected to as encompassing non-elected subject matter.

The Office Action alleges that Margineanu *et al.* (Margineanu) and Shorvon *et al.* (Shorvon) are prior art disclosing the elected species. However, Applicants respectfully point out that Margineanu does not anticipate the claimed invention and does not render obvious the claimed invention, as discussed below. Regarding Shorvon, the Office Action has not rejected the claims as being anticipated or rendered obvious by Shorvon. Moreover, Shorvon does not disclose each of the steps recited in the claims, and therefore does not disclose the claimed invention.

Rejections Under 35 U.S.C. § 112, First Paragraph

A. Claims 93-102, 126-137, and 139-156 are rejected under 35 U.S.C. 112, first paragraph, because the specification allegedly does not enable the claimed invention.

Without acquiescing to the propriety of the rejection of claims 126-137, Applicants have canceled claims 126-137. However, Applicants respectfully point out that claims 126-137 are directed to using the compound or agent identified in claim 93 for measurement of transport across the membrane. Claims 126-137 are not directed to measuring transport across the membrane using a cell free or a membrane free system as alleged by the Office Action.

The Office Action alleges that the claims are not enabled for "fragments" of SV2 proteins or for identifying compounds for treating neurological disorders and endocrinological disorders. In the interest of advancing prosecution of this application, claims 93, 139, and 156 have been amended to delete "a fragment thereof." Claims 139 and 156 have also been amended to delete "endocrinological disorders" and to recite specific neurological disorders.

Claim 93 as it stands is directed to a method of identifying an agent or compound that binds an SV2 protein. Claim 93 comprises the steps of obtaining a cell-free or membrane-free

SV2 protein, incubating the compound or agent with the SV2 protein, and determining whether the compound or agent binds the SV2 protein by comparing its binding to the SV2 protein with LEV's binding to the SV2 protein. Each of these steps is described in detail by the specification, and the specification teaches obtaining cell-free or membrane-free SV2 proteins.

Claims 139 and 156 as they stand are directed to a method of identifying a compound or agent useful for the treatment of neurological disorders such as epilepsy, epileptogenesis, seizure disorders, convulsions, withdrawal seizures, tics, movement disorders, tremor, bipolar disorder, mania, migraine, and chronic or neuropathic pain. Claims 139 and 156 comprise the step of obtaining a cell-free or membrane-free SV2 protein, incubating the compound or agent with the SV2 protein and LEV or an analog or derivative thereof, and determining whether the compound or agent competes with LEV or an analog or derivative thereof for binding to the SV2 protein thereby identifying a compound or agent useful for treating the specifically recited diseases. Each of these steps is taught by the specification, and the specification teaches obtaining cell-free or membrane-free SV2 proteins.

Moreover, as discussed in the previous response, dated September 13, 2006, SV2 proteins are a well known family of synaptic vesicle proteins. They are structurally and functionally related proteins. As an example, the specification shows that SV2A binds to LEV or its analogs or derivatives. Further, published U.S. Application 20050137241 provides further support that SV2 proteins bind LEV (see attached). Example 21 of published U.S. Application 20050137241 shows that the SV2C protein binds LEV or its analogs or derivatives. Accordingly, since SV2 proteins have been characterized and since the specification teaches and the relevant art shows that LEV and its analog or derivatives bind SV2 proteins, the specification enables each of the steps encompassed by the claims and the claimed invention of identifying compounds or agents that bind SV2 or for treating neurological disorders.

The Office Action also alleges that the specification fails to teach that LEV analogs and derivatives (other than LEV L059, LEV analog UCB 30889, and UCB 101282-1) are able to bind SV2 protein. LEV analogs are well known to a person of ordinary skill in the art. Representative examples of LEV analogs or derivatives are provided by the specification, especially on pages 18 to 20. The specification provides assays for determining whether an analog or a derivative of LEV binds a SV2 protein. Also, as discussed above, published U.S.

Application 20050137241 provides further support that SV2 proteins bind LEV and its analogs and derivatives. Accordingly, the specification provides sufficient guidance and examples to enable a person of ordinary skill in the art to determine whether a LEV analog or derivative binds a SV2 protein and can be used in the claimed assay.

Applicants point out that MPEP 2164.02 states, "Compliance with the enablement requirement does not turn on whether an example is disclosed." Also, the specification need not contain an example if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without undue experimentation. *In re Borkowski,* 422 F.2d 904, 908, 164 USPQ 642, 645 (CCPA 1970). As discussed above, the application provides sufficient guidance throughout the specification to enable the skilled artisan to practice the invention with LEV analogs and derivatives without undue experimentation.

Additionally, LEV has been approved by the FDA for treating epilepsy. Epilepsy, epileptogenesis, seizure disorders, convulsions, and withdrawal seizures are well known as diseases related to epilepsy. Therefore, at a minimum, the specification enables the use of the claimed invention for identifying agents useful for treating these disorders. Applicants respectfully point out that as discussed in the previous response, dated September 13, 2006, published PCT application 02/067931 discloses the use of LEV and its analogs and derivatives to treat tics, movement disorders, and tremor, and U.S. Patent 6,903,130 shows that LEV is useful for treating bipolar disorders, mania, migraine, and chronic and neuropathic pain (see claims). Since the use of LEV and its analogs to treat the diseases recited in claims 139 and 156 is well known and given the guidance from the specification for identifying new compounds and agents for treating neurological disorders by comparing the interaction of a test agent with an SV2 protein and that of LEV with an SV2 protein, it is within the skill of the artisan to use the claimed invention to identify compounds and agents for treating neurological disorders recited in claims 139 and 156. Thus, the specification enables the claimed invention.

Applicants respectfully point out that the initial burden is on the Examiner to provide a reasonable explanation as to why the scope of protection provided by the claim is not adequately enabled by the disclosure. *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). Moreover, the court in *In re Marzocchi* stated that it is incumbent upon the Patent Office to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to

back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971). The Office Action has not provided a reasonable explanation as to why the scope of the claims are not adequately enabled by the specification and has not provided evidence showing that the claims as they stand are not enabled by the specification.

B. Claims 93-102, 126-137 and 139-156 are rejected under 35 U.S.C. § 112, first paragraph as failing to meet the written description requirement.

As discussed in the previous Office Action, the claims as they stand are directed to methods of identifying compounds or agents that interact with the SV2 protein. The claims use an SV2 protein comprising an LBS for identifying new compounds or agents that interact with SV2 proteins. The compounds or agents identified by the claimed method may be a LEV analog or derivative. However, the claims are not directed to analogs or derivatives of LEV.

Applicants respectfully submit that the application provides an adequate description of LEV analogs and derivatives throughout the specification. Representative examples of LEV analogs and derivatives are disclosed and described in detail on pages 18-20. Pages 18-20 of the specification also describe in detail the structure for LEV analogs and derivatives. Therefore, the specification discloses defined structures for LEV analogs and derivatives and provides an adequate description of the compounds encompassed by the phrase "LEV analogs and derivatives."

Moreover, U.S. Patent 6,903,130 (which claims priority to WO 01/39779) and published PCT Application 02/067931 disclose various LEV analogs and derivatives. Thus, LEV analogs and derivatives are well known in the art.

Further, given the examples of LEV analogs and derivatives disclosed in the specification, the description of LEV analogs and derivatives provided by the specification, and the disclosure of LEV analogs and derivatives in the relevant art, the specification provides an adequate description of LEV analogs and derivatives. Additionally, based on the description provided by the specification of LEV analogs and derivatives, it is within the skill of an artisan to determine whether a compound is a LEV analog or derivative and whether it can be used in the claimed invention.

Applicants respectfully point out that the claims require that the compound or agent interacts with an SV2 protein. Moreover, claim 93 requires comparing the binding of the compound or agent to an SV2 protein with the binding of LEV to the SV2 protein, and claims 139 and 156 require the addition of LEV or an analog and derivative of LEV to compete with the compound or agent for binding to the LBS on the SV2 protein. LEV as well as its analogs and derivatives are well known compounds and are disclosed and described in the specification. Accordingly, the specification provides an adequate description of LEV analogs and derivatives for the claimed invention.

Rejections Under 35 U.S.C. § 112, Second Paragraph

A. Claims 93-102, 139-156, and 173 are rejected under 35 U.S.C. § 112, second paragraph as incomplete for omitting essential steps.

Applicants respectfully point out that the claims recite all the steps required for identifying an agent that binds an SV2 protein or for treating a neurological disorder. The claims include a step that involves comparing the binding of the agent to an SV2 protein with that of LEV to an SV2 protein or that involves competition between the agent and LEV for binding an SV2 protein. Moreover, the specification describes in detail how to perform each of the steps. Thus, the claims are complete as they stand.

The Office Action alleges that the claims fail to include a step for measuring or detecting the effects of a test compound on any activity of SV2. However, it is not clear the reason that such a step is needed in the claimed methods.

B. Claims 93, 130-132, 135, 137, and 139 are rejected under 35 U.S.C. § 112, second paragraph as being indefinite for reciting "modulate an activity."

Without acquiescing to the propriety of this rejection, Applicants have deleted the phrase from the claims.

Obviousness-Type Non-Statutory Double Patenting Rejection

Claims 93-102, 139-154, and 156 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4, 9-12, 17-19, 22-25, 29, 35, 37-40, 45-52, 54-57, 61-68, 71-74 and 78 of U.S. Patent 7,090,985 ('985).

The claims as they stand are directed to a method of identifying an agent that bind an SV2 protein or is useful for treating a neurological disease. One of the steps comprises obtaining a cell-free or membrane-free SV2 protein. In contrast, the claims of U.S. Patent '985 are directed to a method of identifying a binding partner for SV2A protein comprising providing a recombinant host cell expressing the SV2A protein and incubating the host cell with a test agent and LEV or an analog or derivative thereof. The claims of U.S. Patent also include obtaining a cellular preparation from the host cell and incubating the cellular preparation with a test agent and LEV or an analog or derivative thereof. The claims of U.S. Patent '985 do not require obtaining a cell-free or membrane-free SV2 protein.

The Office Action alleges that a method of screening for a compound using a cell-free or membrane-free polypeptide in a cell-free assay is routine practice. However, SV2 proteins have 12 transmembrane domains and are difficult to obtain in cell-free or membrane-free form for performing screening assays. Applicants discovered a method of obtaining cell-free or membrane-free SV2 proteins useful for performing screening assays. The method is described in detail in the specification.

The Office Action alleges that WO 2003016475 teaches using cell-free or membrane-free polypeptides in high throughput screening assays is routine practice. Although WO 2003016475 generally teaches solubilizing membrane bound proteins, the reference does not teach isolating cell-free or membrane-free SV2 proteins containing twelve transmembrane domains for use in screening assays. The isolation of cell-free or membrane-free SV2 proteins is not routine practice.

Moreover, Applicants respectfully point out that in the parent application (U.S. Patent 7,090,985), claims directed to methods of using isolated and purified SV2 proteins were not allowed because the Examiner alleged that Applicants have not enabled purifying the SV2 protein from the membrane of a cell.

Accordingly, Applicants respectfully request withdrawal of the rejection.

Rejection Under 35 U.S.C. § 102

Claims 93, 97, 99, and 102 are rejected under 35 U.S.C. § 102(e) as being anticipated by WO2003016475 (WO '475).

The Office Action alleges that WO '475 teaches a cell-free screening assay using a cell-

free or membrane-free SV2 protein. Applicants believe that the Office Action is referring to page 961 for disclosing cell-free assays. However, Applicants respectfully point out that WO '475 does not each isolating an SV2 protein from the membrane of a cell and using the isolated SV2 protein in screening assays. Although, WO '475 discloses the SV2A protein sequence as one of the three thousand or so sequences in its Sequence Listing, the phrase "SV2 protein" is not found in the text of WO '475. WO '475 provides general guidance for solubilizing membrane bound proteins, but does not disclose isolating an SV2 protein from the membrane of a cell. Accordingly, WO '475 does not teach or disclose screening assays using cell-free or membrane-free SV2 proteins for performing screening assays to identify compounds or agents that bind SV2 proteins. Moreover, SV2 proteins contain twelve transmembrane domains and are difficult to isolate from the cell membrane in functional form for use in screening assays.

Additionally, the claims require comparing the binding of the agent or compound to SV2 protein with the binding of LEV to SV2 protein. WO '475 does not disclose that SV2 protein interacts with LEV or its analog or derivative. Thus, WO '475 does not teach such a step in the screening assay.

Thus, WO '475 does not anticipate the claimed invention.

Rejections Under 35 U.S.C. § 103

A. Claims 93-102 and 139-156 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO2003016475 (WO '475) in view of Margineanu *et al.* (Margineanu) and Berkower.

The deficiencies of WO '475 are discussed above. The Office Action alleges that WO '475 teaches an assay using cell-free or membrane-free SV2 protein. However, as discussed above, SV2 proteins are not mentioned in the text of WO '475. WO '475 only discloses the amino acid sequence of SV2A in its Sequence Listing as one of the three thousand or so sequences. The reason for the disclosure of SV2 protein sequence in WO '475 is not known. Moreover, WO '475 does not teach how to obtain cell-free or membrane-free SV2 proteins. Further, since SV2 proteins contain 12 transmembrane domains, there is no reasonable expectation of success in isolating SV2 proteins from a cell membrane by following the general information provided by WO '475 for solubilizing membrane bound proteins. Additionally, WO '475 does not disclose that SV2 proteins interact with LEV or its analogs or derivatives.

Likewise, the secondary references Margineanu and Berkower do not disclose LEV binds SV2 proteins. Moreover, these secondary references neither disclose assays using cell-free or membrane-free SV2 protein nor provide guidance for isolating SV2 proteins from cell membranes for use in screening assays to identify new compounds or agents that bind SV2 protein or for the treatment of neurological diseases. Accordingly, since neither the primary nor the secondary references teach that LEV binds SV2 proteins, there is no motivation to combine the three references. Also, since the secondary references do not cure the deficiencies of the primary references, the combination of the three references would not render the claimed invention obvious.

The Office Action alleges that the motivation to combine can arise from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Applicants respectfully point out that the claims as they stand require either comparing the binding of the agent or compound to a SV2 protein with the binding of LEV to the same SV2 protein or having the agent or compound compete with LEV for binding. However, the cited references do not teach that SV2 proteins interact with LEV. Thus, one would not reasonably expect LEV to bind SV2 proteins or to compete with other agents for binding SV2 protein. Thus, there is no motivation to combine the cited references and to modify the teachings of the cited reference to obtain each of the steps of the claimed method.

Additionally, there is no reasonable expectation of success in obtaining cell-free or membrane-free SV2 proteins based on the general disclosure of WO '475 for solubilizing membrane bound proteins, since SV2 proteins contain twelve transmembrane domains. Thus, the cited references do not render the claimed invention obvious.

B. Claims 93 and 126-137 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO2003016475 (WO '475) in view of Xu *et al.* (Xu) and Son *et al.* (Son).

The deficiencies of WO '475 are discussed above. Likewise, the secondary references Xu and Son do not disclose LEV interacts with SV2 proteins. Moreover, these secondary references neither disclose assays using cell-free or membrane-free SV2 proteins nor provide guidance for isolating SV2 proteins from cell membranes for use in screening assays to identify

new compounds or agents that bind SV2 protein or for the treatment of neurological diseases.

Further, the claims require comparing the binding of the agent or compound to SV2 protein with the binding of LEV to an SV2 protein. Neither the primary reference nor the secondary references disclose that SV2 proteins bind LEV or its analog or derivative.

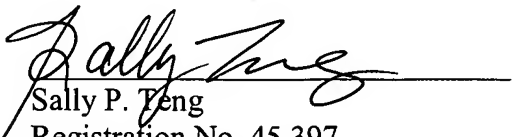
Accordingly, the cited references do not render the claimed invention obvious.

Conclusion

The foregoing amendments and remarks are being made to place the application in condition for allowance. Applicants respectfully request entry of the amendments, reconsideration, and the timely allowance of the pending claims. A favorable action is awaited. Should an interview be helpful to further prosecution of this application, the Examiner is invited to telephone the undersigned.

If there are any additional fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 50-0310. If a fee is required for an extension of time under 37 C.F.R. §1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,
Morgan, Lewis & Bockius LLP



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Date: March 28, 2007
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